Deep learning for detecting BRCA mutations in high-grade ovarian cancer.

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Session Meilleures Communications Orales
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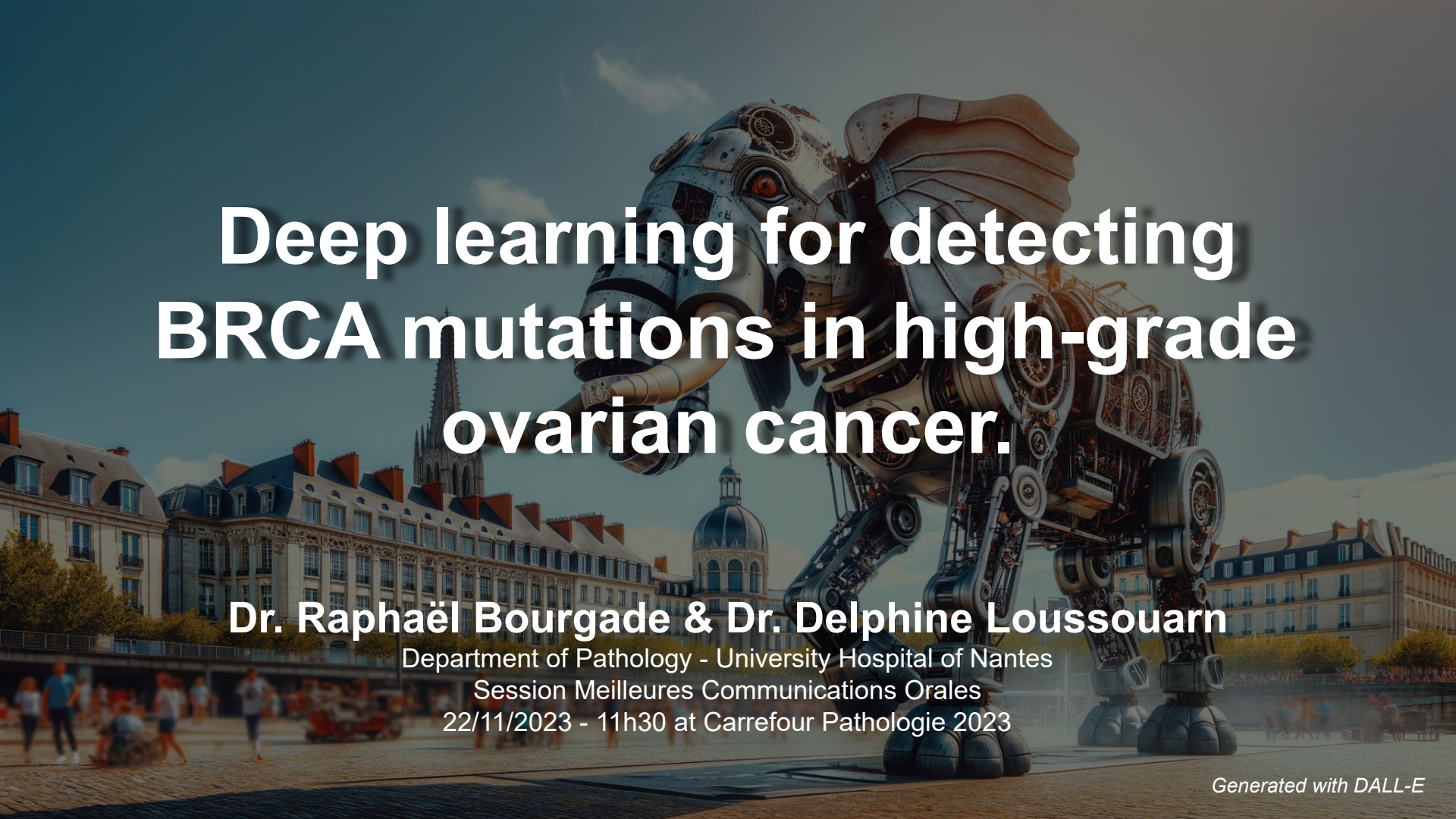

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Introduction

Medical context :

- **~50%** of patients with high-grade serous ovarian cancer have an **Homologous Recombination Deficiency (HRD)**.
- HRD occurs through diverse mechanisms, including mutations in DNA repair genes (most frequently ***BRCA1/2***).
- *BRCA* mutations are **predictive markers** for response to **PARP inhibitors**.
- Currently screened by **NGS** with a few limits → interest of AI ?

Objective :

- Predicting ***BRCA* mutational status** from deep learning analysis of a WSI of high-grade ovarian cancer (HGOC).

Related works :

- Ho *et al.* have achieved **AUC = 0.4 - 0.43** on an internal testset *(Journal of Pathology Informatics, 2023)*
- Nero *et al.* have achieved **AUC = 0.55** on an internal testset *(International Journal of Molecular Science, 2023)*

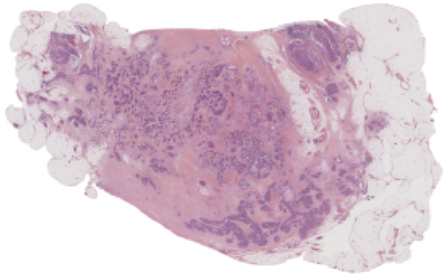
OvarIA dataset :

- **585** slides from Nantes (France)
- **317** slides from Rennes (France

169 BRCA mutated (18,7%)
698 BRCA wild-type (77,4%)
28 Variant of Uncertain Significance (3,1%)
7 Corrupted slides (0,8%)

Sample types :

- Inclusion of **high-grade serous** and **high-grade endometrioid** subtypes.
- Exclusion of **mucinous** subtypes.
- Organs concerned: **peritoneum, ovary, fallopian tube**, and **metastases** site (omentum, node, colon, rectum, ileum, lung, liver, uteri).



HES slide of HGSOC from Nantes

Tumor Segmentation

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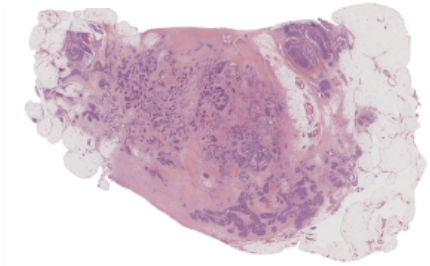
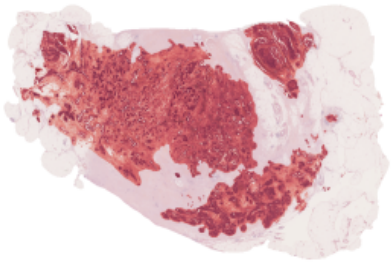
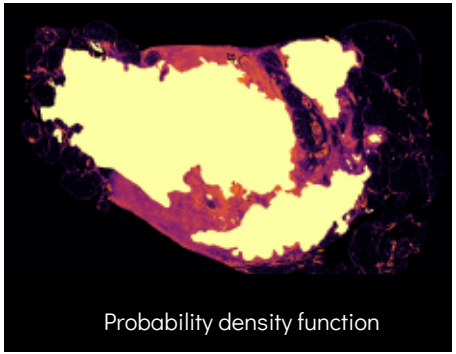
TRAINING



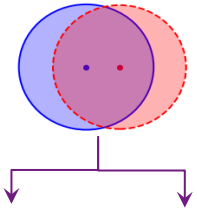
Original HES WSI



Hand-annotated tumor mask



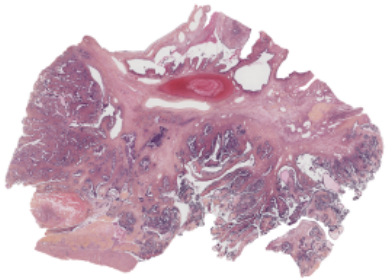
Probability density function



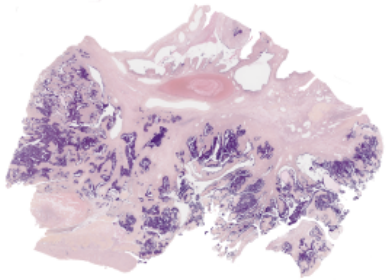
Dice score **0.915**

IoU **0.847**

PREDICTION

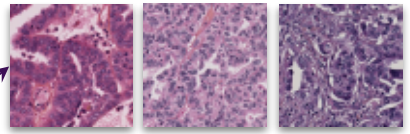


Original HES WSI



Predicted tumor mask

Tumor tiling (th>0.5)



1,687,569 tumor tiles

Classification
1,087M (65%)

SSL
600K (35%)

Feature extraction & Classification

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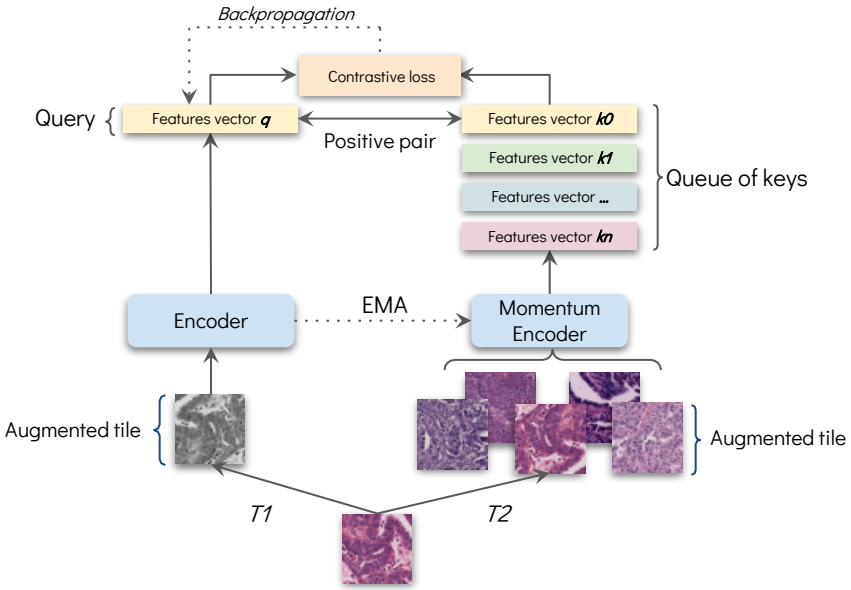
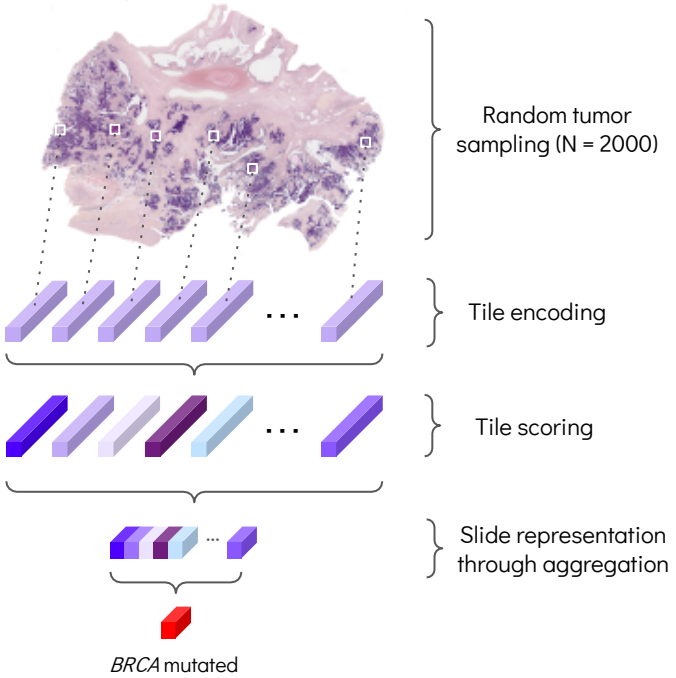
Self-supervised learning:

- **Momentum contrastive** learning (MoCo).
- The **contrastive loss** function **maximizes** similarity of positive pairs while **minimizes** it for negative pairs.

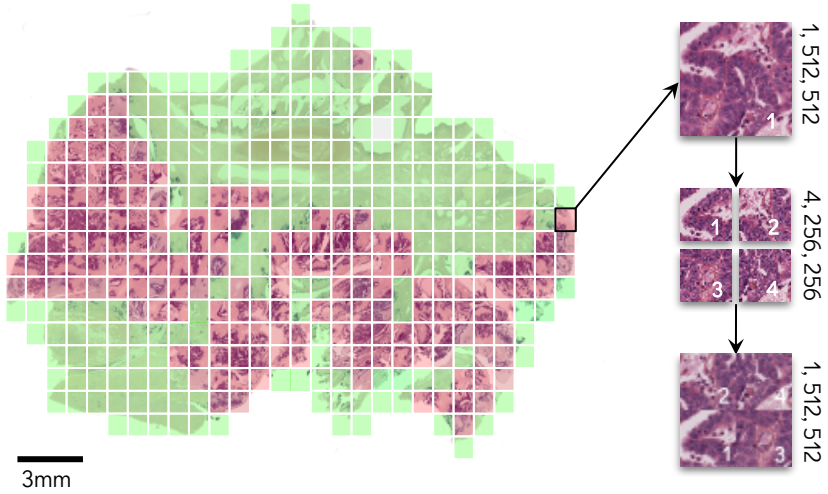


Multiple Instance Learning (MIL) :

- No intuition about the most predictive morphological patterns.
- Attention mechanism increase **interpretability**.



Results



- **State-of-the-art AUC** in *BRCA* prediction (**AUC = 0.43** for Ho *et al.* and **AUC = 0.55** for Nero *et al.*).
- *BRCA* mutations probably have a **phenotypic impact** in HGOC.
- The relevant information seems to reside more in the **tumor spatial conformation** than in the cell morphology.
- It could be interesting to apply this methodology to an **HRD** HGOC cohort.

Acknowledgements

MODERN PATHOLOGY

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Journal homepage: https://modernpathology.org/

Research Article

Deep Learning for Detecting *BRCA* Mutations in High-Grade Ovarian Cancer Based on an Innovative Tumor Segmentation Method From Whole Slide Images

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Acknowledgements

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Thank you for your attention !

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